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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,959	06/25/2001	Richard Ian Christopherson	DAVI139.001C1	2583

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 11/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,959	CHRISTOPHERSON ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1,2 and 17-23 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1,2 and 17-23 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Please note that the examiner assignment has changed for this application.

This response is in reply to the amendment filed August 15, 2005.

Claims 7-17 have been canceled. Claim 1 has been amended. Claims 22 and 23 have been added. Claims 1, 2 and 17-23 are pending and under consideration.

Sections of Title 35, U.S. Code not found in this action can be found in a previous action.

Claims 1, 2, 18, 19, 21, 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method wherein the sample is tissue fluid, blood, CSF, lymphatic fluid, seminal fluid, tumor aspirate, bone marrow aspirate and mucus and the patient is human, does not reasonably provide enablement for the method wherein the biological sample is generic "cells", cell debris, cell extracts serum, plasma, urine and generic aspirate, or a patient which is a "non-human animal". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..
The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(A) As drawn to the method requiring samples which are cell debris, cell extracts, serum, plasma, urine.

Claim 19 requires that the biological sample used for the detection of leukemia is generic "cells", cell debris, cell extracts, serum, plasma, urine and generic "aspirate".

The instant method requires the binding of antibodies to cluster of differentiation antigens, HLA-DR, KOR and/or FMC7 on the surface of leukocytes in order to diagnose the presence leukemia cells in said samples. Thus, it would be necessary to have samples of cells with intact cell membranes because surface proteins are required. Cell extracts are without intact cell membranes, and serum and plasma are biological samples which have been depleted of leukocytes (Dictionary of Immunology, Third Edition, 1985, W.J. Herbert et al, Ed.s, page 199) and therefore would not be expected to have leukemia cells for binding to the antibodies in Table 4. Further, there is no guarantee that "cell debris" would provide a diagnostic target for antibodies which have been raised to cell surface markers because cell debris are damaged and fragmented cells, and the result of said damage on the interaction between a cell membrane of a leukemia cell and an antibody cannot be predicted. Further, claim 14 also requires that the biological sample be "urine". While the art recognizes that detection of immunoglobulins in urine can be diagnostic for leukemia (Wrightman et al, Blood. 1987, Vol. 69, pp. 919-923), the art also teaches that invasion of the bladder by leukemic cells is very rare (the abstract of Chang et al, J Pediatr Hematol Oncol. 2003, Vol. 25, pp. 735-739). Thus there would be no reasonable expectation of success for the detection of leukemic cells in a biological sample which is urine, because leukemic invasion is very rare in the bladder.

(B) As drawn to the method requiring biological samples which are generic "cells", generic "aspirates".

The instant method requires that the method be able to detect leukemia cells. When given the broadest reasonable interpretation, "cells" encompass any cells in a subject. Although it is recognized in the art that leukemia can invade many organs and the central nervous system, there are some organs in which said invasion is rare or not recognized. For instance, Wrightman et al, (ibid) teaches that invasion of the bladder by leukemic cells is very rare. Thus, there would be no reasonable expectation that bladder "cells" would provide a source of leukemic cells for the instant method. Regarding the generic "aspirates", the art teaches that malignant myeloid blast cell can occasionally form solid masses outside of the hemaopoietic system (Buckland et al, Pathology. 2001 Aug Vol. 33, pp. 386-389). However, the term "aspirate" in the claims is not linked to a solid tumor and encompasses an aspirate of any tissue or organ, irrespective of the

presence of a suspicious mass. One of skill in the art would be subject to undue experimentation in order to ascertain the presence of leukemia cells in any biological sample that was an aspirate. (C) As drawn to subjects who are non-human animals.

Claim 23 requires that the subject is a non-human animal. When given he broadest reasonable interpretation reads on the detection of leukemia cells in any non-human animal beyond that of rats, mice and rabbits. The art teaches monoclonal antibodies which bind to cluster of differentiation antigens and other cell surface antigens which are diagnostic for human leukemia. Neither the specification nor any art of record is provided to teach cluster of differentiation antigens and cell surface antigens which are diagnostic for leukemia in the broadly claimed "non-human animal". One of skill in the art would be forced into undue experimentation to determine the homologous antigens on Table 4 in species such as a cat, wherein prior to the date at which priority is sought, the homologous versions of CD 3, 4, 5, 8, 9, 13, 45 and 57 were known along with antibodies that bind thereto. However, there are no teachings in the specification nor any art of record correlating the presence or absence of CD 3, 4, 5, 8, 9, 13, 45 and 57 with the presence or absence or leukemia in the cat. One of skill in the art would be forced into undue experimentation in order to determine the homologues of all the cluster of differentiation antigens and cell surface markers of claim 4 in the cat and then correlate the presence or absence of said marker with the presence or absence or leukemia in the cat. Further, the claims to a non-human animal encompass a multitude of species beyond that of the cat such as animals of the genus Bos and Ursus. One of skill in the art would be forced into undue experimentation to identify the homologous antigens from Table 4 in said animals and determine the association between the presence or absence of cells having these antigens with the presence or absence of leukemia in said animal.

Claims 1, 2, 19, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg et al (JACS, 1995, Vol. 117, pp. 12050-12057) in view of the Becton Dickenson Acute Leukemia Phenotyping Kit, 1992, pages 1-~~92~~ 57

KMC 11/14/05

Claim 1 is drawn to a method for identifying a leukemic T cell, B cell or myeloid lineage cell in a subject comprising contacting a biological sample comprising leukocytes with an array of immunoglobulin molecules immobilized on a solid support, wherein the immunoglobulin

molecules are specific for cell surface marker antigens, wherein the cell surface marker antigens comprise at least seven cell surface marker antigens selected from the list in Table 4, and wherein the cell surface marker antigens distinguish leukemias of T cell, B cell or myeloid lineage, and determining which cell surface marker antigens have bound to which immobilized immunoglobulin molecules to establish a differential pattern of binding that identifies a leukemia that is of T, B or myeloid lineage. Claim 2 embodies the method of claim 1 wherein the immunoglobulin molecules are monoclonal antibodies. Claims 20 and 21 embody the method of claim 1 and 19 respectively, wherein the biological sample is blood. Claim 22 embodies the method of claim 1 wherein the subject is human.

Sundberg et al teach a general method of immobilizing antibodies at precise locations on solid supports, which include glass microscope slides (page 12050, second column, second paragraph and page 12053, under the heading of "Photodeprotection of Caged Biotin Derivatized Slide"). Sundberg et al teach that the technique is amenable for creating a patterned array with a high degree of spatial orientation (page 12050, first column, lines 7-13 under the heading of "Introduction"). Sundberg et al suggest that the technique will be useful in diagnostics (abstract, last two lines). Sundberg et al do not teach the diagnosis of leukemia or the detection of leukemic cells by using the patterned array of antibodies.

Beckton Dickinson teach a kit comprising 12 monoclonal antibodies, and patterns of antibody binding which are indicative of various types of leukemias. Becton Dickenson teach the staining of cells by two antibodies at a time and the separation of antibody pairs by separate tubes (page 4) for analysis by flow cytometry . Becton Dickenson do not teach the use of a patterned antibody array comprising said monoclonal antibodies.

It would have been prima facie obvious at the time the claimed invention was made to use the antibodies taught by Becton Dickenson to be indicative of leukemic cells as a patterned array taught by Sundberg et al. One of skill in the art would have been motivated to do so in order to eliminate the expense of the flow cytometer. One of skill in the art would understand that all the antibodies can be made into a patterned array on the surface of a microscope slide for a single image analysis, eliminating the need for performing a separate flow cytometric analysis on all seven tubes as dictated by Becton-Dickenson. Thus, sampling error and processing time is

decreased, and the requirement for purchasing/maintaining a flow cytometer is eliminated, making the diagnosis faster and more economical.

Claims 1, 2, 18, 19, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg et al (JACS, 1995, Vol. 117, pp. 12050-12057) and the Becton Dickenson Acute Leukemia Phenotyping Kit, 1992 as applied to claims 1, 2, 19, 20 and 22 above, and in further view of Paul (Fundamental Immunology, (text) 1993, page 460).

Claim 18 embodies the method of claim 1 wherein the immunoglobulins are polyclonal. Paul teaches the advantages of polyclonal antibodies over monoclonal antibodies in diagnostics. It would have been prima facie obvious at the time the clamed invention was made to substitute polyclonal antibodies for the monoclonal antibodies which bind to the cell surface antibodies taught by the Becton Dickenson. One of skill in the art would have been motivated to do so by the teachings of Paul.

Claims 1, 2, 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg et al (JACS, 1995, Vol. 117, pp. 12050-12057) and the Becton Dickenson Acute Leukemia Phenotyping Kit, 1992 as applied to claims 1, 2, 19, 20 and 22 above, and in further view of Terstappen et al (US6265150).

Claim 21 embodies the method of claim 19 wherein the immunoglobulin molecules are antigen binding fragments of immunoglobulin molecules.

Terstappen et al teach a method of rapidly obtaining human antibodies against known and novel surface antigens in their native configuration, expressed on phenotypically defined subpopulations of cells from wherein the library of phage particles expressing Fab or single chain Fv (scFv) antibody fragments (claims 1 and 6), wherein said method is a subtracting procedure and does not depend on immunization procedures or the necessity to repeatedly construct phage antibody libraries (abstract).

It would have been prima facie obvious at the time he claimed invention was made to use a library of phage particles expressing Fab or single chain Fv (scFv) antibody fragments to

identify phage particles which bind to the cell surface antigens taught by Becton Dickenson to be diagnostic for leukemia. One of skill in the art would have been motivated to do so in order to clone phage which will be a renewable source of antibody fragments which bind to the antigens require in the patterned array without immunization procedures or repeated construction of antibody libraries.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
11/14/2005

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PRIMARY EXAMINER